



PATENT
Customer No. 22,852
Attorney Docket No. 5725.0903-00

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

In re Application of:)
)
 Shinichi YAMADA et al.)
)
 Application No.: 09/857,495) Group Art Unit: 1617
)
 Filed: June 28, 2001) Examiner: G. Yu
)
 For: COSMETIC COMPOSITION)
)
) COMPRISING AT LEAST A CATION, A)
)
) LIQUID FATTY ALCOHOL AND AT)
)
) LEAST A CERAMIDE TYPE)
)
) COMPOUND AND METHOD USING)
)
) SAME)

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Sir:

APPEAL BRIEF UNDER 37 C.F.R. § 1.192

In support of the Notice of Appeal filed August 11, 2003, the period for response having been extended five months to March 11, 2004, by the accompanying petition and fee, and pursuant to 37 C.F.R. § 1.192, Appellants present in triplicate this brief and encloses herewith a check for the fee of \$320.00 required under 37 C.F.R. § 1.17(c).

This Appeal is filed in response to the final rejection dated April 9, 2003, of claims 19-81, which are set forth in the attached Appendix. If any

additional fees are required or if the enclosed payment is insufficient, Appellants request that the required fees be charged to Deposit Account No. 06-0916

Real Party In Interest

L'Oréal S.A. is the assignee of record.

Related Appeals and Interferences

Appellants' undersigned legal representative knows of no other appeals or interferences that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

Status Of Claims

Claims 19-81 are at issue in this appeal. No claims have been allowed. Claims 19-81 have been finally rejected under 35 U.S.C. § 103(a).

Status Of Amendments

The preliminary amendment has been entered. The amendment filed January 17, 2003, has been entered. The after-final amendment filed July 9, 2003, has been considered but not entered.

No other amendments under 37 C.F.R. §§ 1.111, 1.114, or 1.116 have been filed.

Summary Of Invention

The invention relates to a cosmetic composition for the treatment of keratinous materials such as hair, comprising at least one cationic surfactant, at

least one liquid fatty alcohol and at least one ceramide-type compound and to the method of nontherapeutic treatment using this composition.

One of the means commonly used for improving the disentangling and softness of this hair consists in using care compositions, and then rinsing the hair with water. The invention relates to hair formulations which make it possible to treat hair damaged by adverse weather conditions or physical (blow drying, combing, and the like) or chemical (dyeing, permanent waving, and the like) hair treatments. See specification, page 1, lines 10-14. In general, these compositions are used after a shampoo, optionally preceded by one of the above treatments. *Id.*, page 1, lines 15-18. There have already been used for this purpose ceramides or glyceroceramides which have been combined with cholesterol esters with the aim of protecting the hair fiber. *Id.*, page 1, lines 21-24. The application of the latter compositions or of the ceramides alone to the hair leads nevertheless to inadequate cosmetic performances, both on wet hair and on dry hair. *Id.*, page 1, lines 24-27. Ceramides are generally formulated in thick compositions (cream or gel) containing thickeners with the aim of improving the stability and the suspension of the ceramides in aqueous compositions. *Id.*, page 2, lines 1-4. Liquid products apply better to the hair and become homogeneously distributed. However, it is difficult to obtain stable aqueous liquid compositions, containing water-insoluble compounds such as ceramide-type compounds. *Id.*, page 2, lines 5-9.

The present inventors have discovered that by using compositions containing at least one cationic surfactant, at least one liquid fatty alcohol in combination with ceramide-type compounds, stable liquid compositions were obtained which exhibited substantial improvement in cosmetic performances both on wet hair and on dry hair. *Id.* at p. 2, lines 10-16. For example, the cosmetic properties such as the property of lending suppleness and sleekness to the fibers with no increase in weight or with no greasy effect, of softness and of glossiness are superior to those of a composition containing a solid fatty alcohol generally used for improving the stability of compositions. Furthermore, this composition does not require an exposure time. *Id.* at p. 2, lines 17-26.

Issues

The issues presented for appeal are:

Whether claim 55 is indefinite under 35 USC § 112, second paragraph for failing to particularly point out and distinctly claim the subject matter which Appellants regard as the invention.

Whether claims 19-29, 32-54, and 56-81 are unpatentable under 35 U.S.C. § 103(a) over *Maubru* (U.S. Patent No. 6,312,674 B1) ("*Maubru*") in view of *Bergmann* (U.S. Patent No. 6,110,450) ("*Bergmann*") and *Dubief* (U.S. Patent No. 6,120,757) ("*Dubief-B*").

Whether claims 30 and 31 are unpatentable under 35 USC § 103(a) over *Maubru* in view of *Bergmann, Dubief-B* as applied to claims 19-29, 32-54, and 56-81 above, and further in view of *Critchley* (U.S. Patent No. 5,198,210) ("*Critchley*").

Whether claim 55 is unpatentable under 35 USC § 103(a) as being obvious over *Maubru* in view of *Bergmann, Dubief-B* as applied to claims 19-29, 32-54, and 56-81 above, and further in view of *Ochiai* (U.S. Patent No. 5,587,155) ("*Ochiai*").

Grouping Of Claims

Each claim of this patent application is separately patentable, and upon issuance of a patent will be entitled to a separate presumption of validity under 35 U.S.C. § 282. For convenience in handling this Appeal, however, the claims will be grouped in as follows:

- 1) Claims 19-29, 32-54, and 56-81 will stand or fall together;
- 2) Claims 30 and 31 will stand or fall together; and
- 3) Claim 55 will stand or fall alone.

The argument section which follows sets forth the reasons why Appellants believe the claims are separately patentable.

Arguments

I. INDEFINITENESS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Office rejected claim 55 under 35 U.S.C. § 112, second paragraph, as being indefinite because “it is not clear whether the term ‘18-methyleicosanoic acid’ is a claimed limitation”. *Final Office Action* dated April 9, 2003, page 2.

Appellants submit that claim 55, as amended by the Response and Amendment filed on January 29, 2003, is not indefinite. Claim 55 further limits claim 54 by reciting that 18-methyleicosanoic acid is the fatty acid to be chosen. One of ordinary skill in the art would understand that claim 55 provides a clear and definite recitation of which fatty acid of claim 54 is to be chosen. Appellants respectfully request reconsideration and withdrawal of the rejection.

II. OBVIOUSNESS UNDER 35 U.S.C. § 103(a)

The independent claims on appeal (claims 19, 57, 64, and 74) recite the common feature of a composition comprising, in a cosmetically acceptable aqueous medium, at least one liquid fatty alcohol, at least one ceramide compound, and at least one cationic surfactant.

In making a rejection under 35 U.S.C. § 103, the Office has the initial burden to establish a prima facie case of obviousness. M.P.E.P. § 2143. To establish a prima facie case of obviousness, the Office must demonstrate, among other things, that there is some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to one of ordinary skill in the art,

to modify a reference or combine reference teachings. M.P.E.P. § 2143.03.

Furthermore, the teaching or suggestion to make the claimed combination must be found in the prior art, not in Appellants' disclosure. See *In re Vaeck*, 20 U.S.P.Q.2d 1438, (Fed. Cir. 1991). For the reasons that follow, Appellants submit that the Office has failed to make a prima facie case of obviousness because it has not met either, let alone both of the above criteria.

A. MAUBRU IN VIEW OF BERGMANN AND DUBIEF-B

The Office maintains the rejection of claims 19-29, 32-54, and 56-81 under 35 U.S.C. § 103(a) as being unpatentable over *Maubru* in view of *Bergmann* and *Dubief-B* for the reasons set forth in the Office Action dated September 24, 2002, and as supplemented at pages 3-5 of the final Office Action dated April 9, 2003. The Office alleges that "given the general teaching in *Maubru* that conventional additives for oxidizing composition for hair can be employed, it would have been obvious to...have looked to the prior arts such as *Bergmann* and *Restle* for specific additives such as fatty alcohol and quaternary ammonium surfactants." ¹ *Final Office Action* dated April 9, 2003, at p. 5.

As a basis for its rejection, the Office alleges that:

The motivation to combine the ingredients to
successfully formulate a hair composition for topical

¹ *Restle* was not cited in statement of rejection so we assume *Dubief-B* was intended by the Examiner.

application is found in the teachings [of] the prior arts that these are old and well known for hair treatment purposes. See In re Kerkhoven. Nothing nonobvious or unexpected is seen in combining conventional ingredients used for the same purposes. See MPEP § 718.02.

Id.

1. Reliance on Kerkhoven is Misplaced

Appellants disagree with the Office's reliance on *Kerkhoven*, introduced in this case by the Office only in the final Office Action dated April 9, 2003, as a short cut means to establishing a prima facie case of obviousness without first establishing the elements of a prima facie case as required by the Supreme Court in *Graham v. John Deere*, 383 U.S. 1(1966). Further, as discussed below, Appellants submit that *Kerkhoven* has been improperly relied upon, and does not support the Office's position.

First, the facts and holding of *Kerkhoven* involved "combin[ing] two compositions each of which is taught by the prior art to be useful for the same purpose." *In re Kerkhoven*, 205 USPQ 1069, 1072 (CCPA 1980) (emphasis added). However, in contrast to *Kerkhoven*, in the present case the Office does not appear to be combining compositions. Rather, in an effort to reproduce Appellants' claimed invention, the Office is picking and choosing individual components from isolated disclosures in the cited references. However, "[s]uch piecemeal reconstruction of the prior art patents in light of [Appellants'] disclosure is contrary to the requirements of 35 U.S.C. 103." *In re Wesslan*, 147 USPQ 391, 393 (CCPA 1965).

Indeed, in order to properly apply *Kerkhoven*, the combination from the three cited references would be: one or more oxidation compositions comprising a ceramide, where the preceding are from *Maubru*; and then from *Bergmann*, at least one ceramide or cationic polymer, phytantriol, and then from *Dubief-B*, at least one quaternary ammonium surfactant. This combination is not the combination made by the Office and therefore *Kerkhoven* is misapplied.

2. No Motivation to Combine in the Rejection

The Office's conclusory statements are not adequate grounds for a rejection based on obviousness. "[P]articular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed." *In re Rouffet*, 149 F.3d 1350, 1359 (Fed. Cir. 1998). Indeed, the Office can satisfy the burden of showing obviousness "only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992).

The Federal Circuit has held that with respect to core factual findings in a determination of patentability, the Examiner "must point to some concrete evidence in the record in support of these findings." *In re Zurko*, 59 U.S.P.Q.2d 1693, 1697 (Fed. Cir. 2001). As the Examiner has failed to provide any concrete evidence in

the record to support the proposed combination, the Examiner has not met the burden to establish a prima facie case of obviousness.

Finally, the Federal Circuit recently has reaffirmed the Examiner's high burden to establish a prima facie case of obviousness and has emphasized the requirement of specificity. See *In re Lee*, 61 U.S.P.Q.2d 1430 (Fed. Cir. 2002). In *Lee*, the Federal Circuit held that "[t]he factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with." *Id.* 61 U.S.P.Q.2d at 1433 (emphasis added).

In this case, the Office has not provided an adequate explanation of why it would have been allegedly obvious to combine the teachings of *Maubru*, *Bergmann*, and *Dubief-B*. Here, the combination fails to provide the requisite motivation necessary to support a prima facie case of obviousness because it does not teach or suggest the inclusion of any ceramide with a quaternary ammonium surfactant in an oxidizing composition. Further, there would have been no reasonable expectation of success for such a combination because *Maubru* does not disclose the utility of ceramides in an oxidizing composition in combination with a quaternary ammonium surfactant, or any surfactants for that matter.

In response to Appellants previous arguments the Office alleges:

[T]he *Bergmann* reference teaches in col. 6, lines 58-62, to use "natural, hydrogenated or unhydrogenated, synthetic or non-synthetic hydrocarbon oils which are cyclic or aliphatic, linear or branched,

saturated or unsaturated and soluble or insoluble, fatty alcohols". In view of this suggestion, examiner takes the position that the selection of liquid fatty alcohol in this case is obvious.

Id. Final Office Action dated April 9, 2003, page 6, emphasis added. Appellants disagree with the Office interpretation of what is allegedly disclosed at col. 6, lines 58-62.

Appellants submit that the disclosure at col. 6, lines 58-62, to "cyclic or aliphatic, linear or branched, saturated or unsaturated" is relative only to "hydrocarbon oils" and is not relative to fatty alcohols. Further, Appellants point out that prior art cosmetic compositions were known to add solid fatty alcohol generally to improve the stability of compositions, for example, due to fatty alcohol's known emulsifying and thickening properties. Specification, page 2, lines 21-23. Appellants, however, have discovered that addition of at least one liquid fatty alcohol in combination with ceramide-type compounds results in stable liquid compositions which exhibit substantial improvement in cosmetic performance on both wet hair and on dry hair. *Id.*, page 2, lines 10-16. There is no evidence of record for making such a composition and neither is there evidence that such a composition would be stable and provide improved performance on hair. Therefore, Appellants' discovery provides additional evidence that one of ordinary skill in the art at the time of invention would not have been motivated by *Bergmann* to add liquid fatty alcohol as proposed by the Office.

3. No Expectation of Success

Further, if the Office is suggesting the combination of compositions, Appellants submit that the Office has no evidence from which it can predict the outcome of such a combination, or have a reasonable expectation of success for the combination. In fact, it is known that dye components can interact to affect the properties of the composition unpredictably, including its toxicity. For example, in C. Zviak, *The Science of Hair Care*, Marcel Kekker, Inc., p. 329 (1986) (copy attached), Zviak explains that, with respect to the safety of finished products, “[a]ll finished cosmetic products must be evaluated for safety in use to make sure that they do not, under normal and foreseeable conditions, constitute a potential hazard for the consumer....” Zviak explains that such testing is not easily accomplished due to unpredictable component interactions. Specifically, “[i]t might seem that a sensible way of proceeding would be to conduct most toxicological tests on the ingredients, which would reduce the amount of experimentation and cost of developing finished products. However, experience has shown that the formulation itself is the important element. It determines local tolerance after a single or repeated application, eye and/ or lung mucosa tolerance, the degree of absorption through the skin, etc.” *Id.* Further, according to Zviak, synergistic effects that make a product more or less toxic may occur. That is, “[a]part from the effect of the vehicle, it has been observed that the association of different compounds can product either

synergistic toxicity or, on the contrary, a mitigation or even inhibition of toxic effects.”

Id.

As a result, Appellants respectfully submit that a prima facie case of obviousness over *Maubru* in view of *Bergmann* and *Dubief-B* has not been established, and accordingly request withdrawal of the rejection.

B. MAUBRU IN VIEW OF BERGMANN, DUBIEF-B, AND CRITCHLEY

The Office has finally rejected claim 30 and 31 under 35 USC § 103(a) as being obvious over *Maubru* in view of *Bergmann*, *Dubief-B* as applied to claims 19-29, 32-54, and 56-81 above, and further in view of *Critchley* (U.S. Patent No. 5,198,210) (“*Critchley*”) for the reasons set forth in the Office Action dated September 24, 2002, and as supplemented at page 5 of the final Office Action dated April 9, 2003. Appellants respectfully traverse the rejection for the following reasons.

For the reasons set forth above, Appellants submit that claims 30 and 31 are also patentable over *Maubru* in view of *Bergmann*, *Dubief-B* as applied to claims 19-29, 32-54, and 56-81, and further in view of *Critchley*. *Critchley* is only cited as teaching compositions containing emollients such as isocetyl alcohol, stearyl alcohol, and cetyl alcohol. *Id.* The remaining three references are applied against these claims as in the rejection discussed above. Appellants incorporate herein by reference the above arguments of why claims 19-29, 32-54, and 56-81 are patentable over *Maubru* in view of *Bergmann*, *Dubief-B*, and apply these arguments

to as applied to *Maubru* in view of *Bergmann*, *Dubief-B*, and further in view of *Critchley*. As Appellants have noted, the Office has identified no evidence of a teaching, suggestion, or motivation to combine those references. *Critchley* does not cure this deficiency.

The Office alleges that it would have been obvious “to have modified the compositions of [*Dubief-B*] by substituting the stearyl alcohol and cetyl alcohol with isocetyl alcohol, as suggested by *Critchley*, because of the expectation of successfully producing hair care products with similar emolliency effects.” *Final Office Action*, dated April 9, 2003, page 9. Appellants respectfully submit that this argument lacks the required motivation and expectation of success and fails to meet the Office’s burden of establishing a prima facie case of obviousness.

Critchley teaches a composition comprising a pseudoceramide and a cosmetically acceptable vehicle. Moreover, *Critchley* teaches wide variety of compounds that are useful as cosmetically acceptable vehicles “to act as a dilutant, dispersant or carrier for the pseudoceramide in the composition, so as to facilitate its distribution when the composition is applied to the skin and/or hair.” Col. 10, lines 32-38. These cosmetically acceptable vehicles are further defined to include any of a multitude of liquid or solid emollients, propellants, solvents, humectants, thickeners, and powders. Col. 10, line 39, to Col. 11, line 11. A few liquid fatty alcohols are included amongst the long list of numerous emollients indicated, which also included numerous solid fatty alcohols and other non-alcoholic emollients.

Thus, a vast majority of the emollients disclosed in *Critchley* would not be a liquid fatty alcohol.

The Federal Circuit requires evidence of a suggestion or motivation to modify the teachings of prior art references. See, e.g., *In re Dembiczak*, 50 USPQ.2d 1614 (Fed. Cir. 1999). Modifying prior art references without evidence of such a suggestion or motivation simply takes the inventor's specification as a blueprint for piecing together the prior art to defeat patentability, i.e., the essence of hindsight. *Id.* at 1617. This is why the Federal Circuit placed the burden on the Office to present "clear and **particular**" **evidence** showing motivation to combine or modify. *Id.* More recently, the Federal Circuit has also held that:

This factual question of motivation is material to patentability, and could not be resolved on **subjective belief and unknown authority**. It is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to '[use] that which the inventor taught against its teacher.' ... Thus the [Office] must not only assure that the requisite findings are made, based on evidence of record, but must also **explain the reasoning** by which the findings are deemed to support the agency's conclusion.

In re Lee, 61 U.S.P.Q.2d at 1433, citations omitted, emphasis added (Fed. Cir. 2002).

Appellants submit that the evidence relied upon by the Office for showing motivation to combine *Maubru*, *Bergmann*, and *Dubief-B*, with a liquid fatty alcohol of *Critchley* to obtain the claimed invention is apparently based solely on subjective belief or unknown authority. As in *Lee*, beyond the conclusory statements of

record, the Office in the outstanding Office Action fails to explain the reasoning supporting the conclusion that one of ordinary skill in the art would have been motivated to use the liquid fatty alcohol emollients of *Critchley*, in combination with *Maubru*, *Bergmann*, and *Dubief-B*, with the expectation of successfully producing a liquid cosmetic composition, comprising, in a cosmetically acceptable medium, at least one liquid fatty alcohol, at least one ceramide compound, and at least one cationic surfactant. In fact, Appellants submit that nothing in *Critchley* would have led one of ordinary skill in the art to select as an emollient a liquid fatty alcohol over the other solid fatty alcohol and non-alcoholic emollients disclosed in the reference.

The Office has failed to present "**clear and particular**" evidence showing motivation to combine or modify as is required in *In re Dembiczak*, nor has the Office provided a **reasoned explanation** as required in *In re Lee*. Thus, the evidence relied upon by the Office does not provide the requisite motivation for one of ordinary skill in the art to devise the Office's proposed combination of *Maubru*, *Bergmann*, *Dubief-B*, and *Critchley*.

Appellants respectfully request reconsideration and withdrawal of the rejection.

C. MAUBRU IN VIEW OF BERGMANN, DUBIEF-B, AND OCHIAI

The Office has finally rejected claim 55 under 35 USC § 103(a) as being obvious over *Maubru* in view of *Bergmann, Dubief-B* as applied to claims 19-29, 32-54, and 56-81 above, and further in view of *Ochiai* (U.S. Patent No. 5,587,155) ("*Ochiai*") for the reasons set forth in the Office Action dated September 24, 2002, and as supplemented at pages 6 of the final Office Action dated April 9, 2003. Appellants disagree with the Office's position. For the reasons set forth above, Appellants submit that claim 55 is also patentable over *Maubru* in view of *Bergmann, Dubief-B* as applied to claims 19-29, 32-54, and 56-81, and further in view of *Ochiai*. Appellants incorporate herein by reference the above arguments of why claims 19-29, 32-54, and 56-81 are patentable over *Maubru* in view of *Bergmann, Dubief-B*, and apply these arguments to as applied to *Maubru* in view of *Bergmann, Dubief-B*, and further in view of *Ochiai*.

Ochiai is only cited as teaching hair conditioning compositions containing 18-methyleicosanoic acid. *Id.* The remaining three references are applied against this claim as in the rejection discussed above. As Appellants have noted, the Office has identified no evidence of a teaching, suggestion, or motivation to combine those references. *Ochiai* does not cure this deficiency.

The Office alleges that it would have been obvious "to have modified the compositions of the combined references by adding a well known hair conditioning ingredient such as 18-methyleicosanoic acid as motivated by *Ochiai*, because of the

expectation of successfully producing hair conditioning composition with enhanced effects." *Final Office Action*, dated April 9, 2003, page 6. Appellants respectfully submit that this argument lacks the required motivation and expectation of success and fails to meet the Office's burden of establishing a prima facie case of obviousness.

Ochiai teaches a hair composition comprising a fatty acid, such as 18-methyleicosanoic acid. Moreover, *Ochiai* teaches a wide variety of other fatty acids that are acceptable for use in their hair composition Col. 2, lines 27-60. Thus 18-methyleicosanoic acid is included amongst the long list of numerous fatty acids indicated.

As emphasized above, the Federal Circuit in *In re Dembiczak* placed the burden on the Office to present "**clear and particular**" evidence showing motivation to combine or modify. Moreover, the Federal Circuit in *In re Lee* also required that the Office findings are deemed to support the agency's conclusion. *In re Lee*, 61 U.S.P.Q.2d at 1433.

Appellants submit that the evidence relied upon by the Office for showing motivation to combine *Maubru*, *Bergmann*, and *Dubief-B*, with 18-methyleicosanoic acid of *Ochiai* to obtain the claimed invention is based only on subjective belief or unknown authority. As in *In re Lee*, beyond the conclusory statements of record, the Office in the outstanding Office Action fails to explain the reasoning supporting the conclusion that one of ordinary skill in the art would have been motivated to use

the 18-methyleicosanoic acid of *Ochiai*, in combination with *Maubru*, *Bergmann*, and *Dubief-B*, with the expectation of successfully producing a aqueous hair composition comprising, in a cosmetically acceptable medium, at least one liquid fatty alcohol, at least one ceramide compound, at least one cationic surfactant, and 18-methyleicosanoic acid. In fact, Appellants submit that nothing in *Ochiai* would have led one of ordinary skill in the art to select 18-methyleicosanoic acid over the other fatty acids disclosed in the reference.

The Office has failed to present "clear and **particular**" **evidence** showing motivation to combine or modify as is required in *In re Dembiczak*, nor has the Office provided a **reasoned explanation** as required in *In re Lee*. Thus, the evidence relied upon by the Office does not provide the requisite motivation for one of ordinary skill in the art to devise the Office's proposed combination of *Maubru*, *Bergmann*, *Dubief-B*, and *Ochiai*.

Appellants respectfully request reconsideration and withdrawal of the rejection.

Conclusion

For the reasons set forth above, Appellants respectfully maintain that a prima facie case of obviousness has not been established by the Office based on the cited references, taken alone or in combination. Thus, Appellants respectfully request reversal of all the rejections of claims 19-81 under 35 U.S.C. § 103(a).

To the extent any further extension of time under 37 C.F.R. § 1.136 is required to obtain entry of this Appeal Brief, such extension is hereby respectfully requested. If there are any fees due under 37 C.F.R. §§ 1.16 or 1.17 which are not enclosed herewith, including any fees required for an extension of time under 37 C.F.R. § 1.136, please charge such fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.



Charles D. Niebylski
Reg. No. 46,116

Date: March 10, 2004

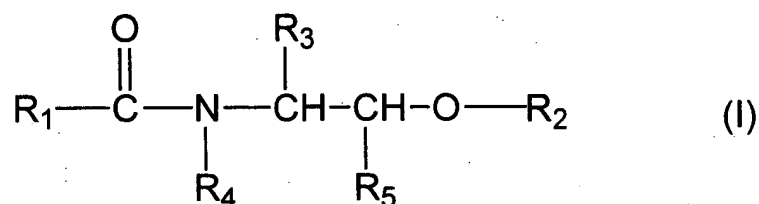
Post Office Address (to which
correspondence is to be sent)

Finnegan, Henderson, Farabow,
Garrett & Dunner, L.L.P.
1300 I Street, N.W.
Washington, D.C. 20005
(202) 408-4000

APPENDIX - PENDING CLAIMS

19. (Previously Presented) A liquid cosmetic composition, comprising, in a cosmetically acceptable aqueous medium, at least one liquid fatty alcohol, at least one ceramide compound and at least one cationic surfactant.

20. (Previously Presented) The composition according to claim 19, wherein said at least one ceramide compound is of formula (I):



wherein:

- R₁ is chosen from:

- a saturated or unsaturated, linear or branched, C₁-C₅₀ hydrocarbon group, wherein said C₁-C₅₀ hydrocarbon group is optionally substituted with at least one hydroxyl group, wherein said hydroxyl group is optionally esterified by an acid R₇COOH, R₇ being chosen from a linear or branched, saturated or unsaturated, C₁-C₃₅ hydrocarbon group, wherein said C₁-C₃₅ hydrocarbon group of R₇ is optionally substituted with at least one hydroxyl group that is optionally esterified by a linear or branched, saturated or unsaturated, C₁-C₃₅ fatty acid, wherein said C₁-C₃₅ fatty acid is optionally substituted with at least one hydroxyl group;

- a group $R''-(NR-CO)-R'$, wherein R is chosen from hydrogen and a C_1-C_{20} hydrocarbon group substituted with at least one hydroxyl group, and wherein R' and R'' are chosen from hydrocarbon groups, wherein the sum of the carbon atoms in R' and R'' ranges from 9 to 30, and wherein R' is a divalent radical; and

- a group $R_8-O-CO-(CH_2)_p$, wherein R_8 is a C_1-C_{20} hydrocarbon group, and p is an integer ranging from 1 to 12;

- R_2 is chosen from hydrogen, a saccharide group, a sulfate residue, a phosphate residue, a phosphorylethylamine group and a phosphorylethylammonium group;

- R_3 is chosen from hydrogen and a saturated or unsaturated, linear or branched, C_2-C_{33} hydrocarbon group, wherein said C_1-C_{33} hydrocarbon group is optionally substituted with at least one hydroxyl group, wherein said hydroxyl group is

- optionally esterified by an acid chosen from an inorganic acid and an acid R_7COOH , wherein R_7 has the same meaning as above, or

- optionally etherified by a group chosen from a (glycosyl) $_n$ group, a (galactosyl) $_m$ group, a sulfogalactosyl group, a phosphorylethylamine group and a phosphorylethylammonium group, wherein n is an integer ranging from 1 to 4 and m is an integer ranging from 1 to 8 ,

and wherein R_3 is optionally substituted with at least one C_1-C_{14} alkyl group;

- R_4 is chosen from hydrogen, a methyl group, an ethyl group, an optionally hydroxylated, linear or branched, saturated or unsaturated, C_3-C_{50} hydrocarbon group, a group $-CH_2-CHOH-CH_2-O-R_6$, wherein R_6 is chosen from a $C_{10}-C_{26}$ hydrocarbon group and a group $R_8-O-CO-(CH_2)_p$, wherein R_8 is a C_1-C_{20} hydrocarbon group, and p is an integer ranging from 1 to 12;

- R₅ is chosen from hydrogen and a saturated or unsaturated, linear or branched, C₁-C₃₃ hydrocarbon group optionally substituted with at least one hydroxyl group, wherein said hydroxyl group is optionally etherified by a group chosen from a (glycosyl)_n group, a (galactosyl)_m group, a sulfogalactosyl group, a phosphorylethylamine group, and a phosphorylethylammonium group, wherein m and n have the same meanings as above; and with the proviso that when R₃ and R₅ are each hydrogen or when R₃ is hydrogen and R₅ is a methyl group, then R₄ is not chosen from hydrogen, a methyl group, and an ethyl group.

21. (Previously Presented) The composition according to claim 20, wherein R₁ is a saturated or unsaturated, linear or branched, C₅-C₅₀ hydrocarbon group.

22. (Previously Presented) The composition according to claim 20, wherein R in group R''-(NR-CO)-R', is a monohydroxylated C₁-C₂₀ hydrocarbon group.

23. (Previously Presented) The composition according to claim 20, wherein R₂ is a saccharide group chosen from a (glycosyl)_n group, a (galactosyl)_m group and a sulfogalactosyl group, wherein n is an integer ranging from 1 to 4 and m is an integer ranging from 1 to 8.

24. (Previously Presented) The composition according to claim 20, wherein R_3 is a C_{15} - C_{26} ∇ -hydroxyalkyl group, wherein the ∇ -hydroxyl group of said ∇ -hydroxyalkyl is optionally esterified by a C_{16} - C_{30} ∇ -hydroxy acid.

25. (Previously Presented) The composition according to claim 19, wherein said at least one ceramide compound is chosen from:

- 2-(N-linoleoylamino)-1,3-octadecanediol,
- 2-(N-oleoylamino)-1,3-octadecanediol,
- 2-(N-palmitoylamino)-1,3-octadecanediol,
- 2-(N-stearoylamino)-1,3-octadecanediol,
- 2-(N-behenoylamino)-1,3-octadecanediol,
- 2-[N-(2-hydroxypalmitoyl)amino]-1,3-octadecanediol,
- 2-(N-stearoylamino)-1,3,4-octadecanetriol, and
- 2-(N-palmitoylamino)-1,3-hexadecanediol.

26. (Previously Presented) The composition according to claim 19, wherein said at least one ceramide compound is chosen from bis(N-hydroxyethyl-N-cetyl)malonamide, N-(2-hydroxyethyl)-N-(3-cetyloxy-2-hydroxypropyl)amide of cetylic acid and N-docosanoyl-N-methyl-D-glucamine.

27. (Previously Presented) The composition according to claim 19, wherein said at least one ceramide compound is present in a concentration ranging from 0.0001% to 20% by weight, relative to the total weight of the composition.

28. (Previously Presented) The composition according to claim 27, wherein said at least one ceramide compound is present in a concentration ranging from 0.001% to 10% by weight, relative to the total weight of the composition.

29. (Previously Presented) The composition according to claim 28, wherein said at least one ceramide compound is present in a concentration ranging from 0.005% to 3% by weight, relative to the total weight of the composition.

30. (Previously Presented) The composition according to claim 19, wherein said at least one liquid fatty alcohol is chosen from lauryl alcohol, isomyristyl alcohol, isostearyl alcohol, isocetyl alcohol, isoarachidyl alcohol, 2-octyldodecanol, 2-butyloctanol and oleyl alcohol.

31. (Previously Presented) The composition according to claim 30, wherein said at least one fatty alcohol is chosen from isostearyl alcohol and isocetyl alcohol.

32. (Previously Presented) The composition according to claim 19, wherein said at least one liquid fatty alcohol is present in a concentration ranging from 0.5% to 10% by weight, relative to the approximate total weight of the composition.

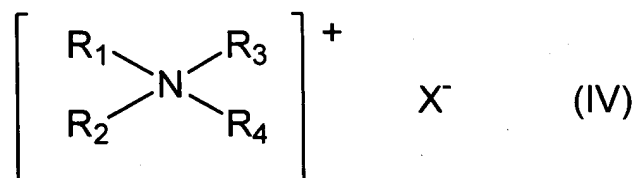
33. (Previously Presented) The composition according to claim 32, wherein said at least one liquid fatty alcohol is present in a concentration ranging

from 1% to 10% by weight, relative to the approximate total weight of the composition.

34. (Previously Presented) The composition according to claim 33, wherein said at least one liquid fatty alcohol is present in a concentration ranging from 1.5% to 3% by weight, relative to the total weight of the composition.

35. (Previously Presented) The composition according to claim 19, wherein said at least one cationic surfactant is chosen from:

A) quaternary ammonium salts of formula (IV):



wherein X^- of formula (IV) is an anion chosen from halide anions, (C₂-C₆)alkyl sulfate anions, phosphate anions, alkyl sulfonate anions, alkylaryl sulfonate anions, and anions derived from an organic acid, and

(i) R_1 , R_2 , and R_3 , of formula (IV), which may be identical or different, are chosen from aromatic groups and from linear and branched aliphatic groups comprising from 1 to 4 carbon atoms, wherein said aliphatic groups optionally comprise at least one heteroatom, and then

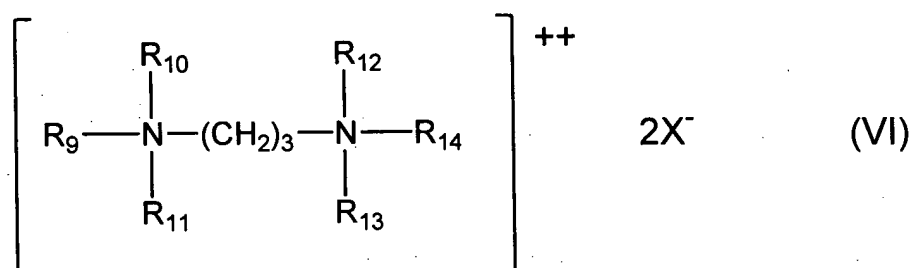
R_4 of formula (IV) is chosen from linear and branched alkyl groups comprising from 20 to 30 carbon atoms; or alternatively

(ii) R_1 and R_2 , of formula (IV), which may be identical or different, are chosen from aromatic groups and from linear and branched aliphatic groups comprising from 1 to 4 carbon atoms, wherein said aliphatic groups optionally comprise at least one heteroatom, and then

R_3 and R_4 , of formula (IV), which may be identical or different, are chosen from linear and branched alkyl groups comprising from 12 to 30 carbon atoms, wherein said alkyl groups comprise at least one group chosen from ester groups and amide groups;

B) - quaternary ammonium salts of imidazolinium;

C) - quaternary diammonium salts of formula (VI):



wherein

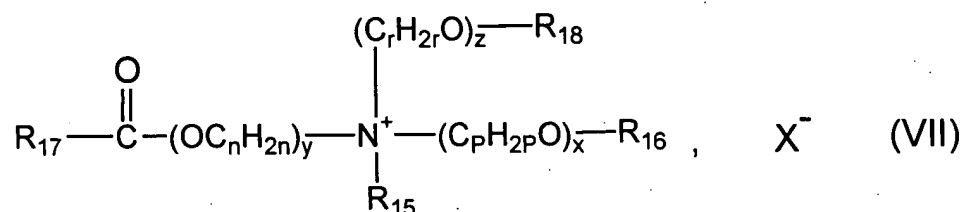
R_9 is chosen from aliphatic groups comprising from about 16 to 30 carbon atoms,

R_{10} , R_{11} , R_{12} , R_{13} and R_{14} , which may be identical or different, are chosen from hydrogen and alkyl groups comprising from 1 to 4 carbon atoms, and

X^- of formula (VI) is an anion chosen from halide anions, acetate anions, phosphate anions, nitrate anions and methyl sulfate anions;

and

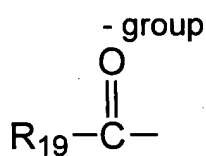
D) - quaternary ammonium salts, comprising at least one ester functional group, of formula (VII),:



wherein

- R₁₅ is chosen from C₁-C₆ alkyl groups, C₁-C₆ hydroxyalkyl groups, and dihydroxyalkyl groups;

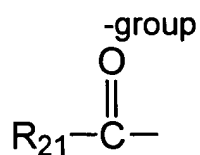
- R₁₆ is chosen from:



- linear and branched, saturated and unsaturated, C₁-C₂₂ hydrocarbon groups R₂₀, and

- hydrogen,

- R₁₈ is chosen from:



- linear and branched, saturated and unsaturated, C₁-C₆ hydrocarbon groups R₂₂, and

- hydrogen,

- R_{17} , R_{19} and R_{21} , which are identical or different, are each chosen from linear and branched, saturated and unsaturated, C_7 - C_{21} hydrocarbon groups;
 - n , p and r , of formula (VII), which are identical or different, are each integers having values ranging from 2 to 6;
 - y of formula (VII) is an integer having a value ranging from 1 to 10;
 - x and z , of formula (VII), which are identical or different, are each integers having values ranging from 0 to 10;
 - X^- of formula (VII) is an anion chosen from organic anions and inorganic anions, and chosen from simple anions and complex anions;
- with the provisos that the sum $x + y + z$, of formula (VII), has a value ranging from 1 to 15, that when x of formula (VII) has a value of 0, then R_{16} denotes R_{20} , and that when z of formula (VII) has a value of 0, then R_{18} denotes R_{22} .

36. (Previously Presented) The composition according to claim 35, wherein said at least one cationic surfactant is chosen from a quaternary ammonium salt of formula (IV) wherein X^- of formula (IV) is an anionic halide chosen from chloride, bromide and iodide.

37. (Previously Presented) The composition according to claim 35, wherein said at least one cationic surfactant is chosen from a quaternary ammonium salt of formula (IV) wherein X^- of formula (IV) is methyl sulfate.

38. (Previously Presented) The composition according to claim 35, wherein said at least one cationic surfactant is chosen from quaternary ammonium

salts of formula (IV) wherein X^- of formula (IV) is an anion derived from an organic acid chosen from acetate and lactate.

39. (Previously Presented) The composition according to claim 35, wherein said at least one cationic surfactant is chosen from quaternary ammonium salts of formula (IV) wherein in (i), R_1 , R_2 and R_3 , of formula (IV), which may be identical or different, are chosen from aryl groups and alkylaryl groups.

40. (Previously Presented) The composition according to claim 35, wherein said at least one cationic surfactant is chosen from quaternary ammonium salts of formula (IV) wherein in (i), R_1 , R_2 and R_3 , of formula (IV), which may be identical or different, are chosen from aliphatic groups comprising at least one heteroatom chosen from oxygen, nitrogen, sulfur, and halogens.

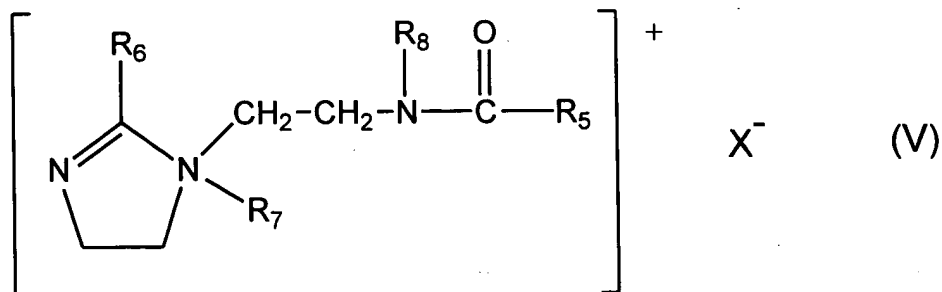
41. (Previously Presented) The composition according to claim 35, wherein said at least one cationic surfactant is chosen from quaternary ammonium salts of formula (IV) wherein in (ii), R_1 and R_2 , of formula (IV), which may be identical or different, are chosen from aryl groups and alkylaryl groups.

42. (Previously Presented) The composition according to claim 35, wherein said at least one cationic surfactant is chosen from quaternary ammonium salts of formula (IV) wherein in (ii), R_1 and R_2 , of formula (IV), which may be identical or different, are chosen from aliphatic groups comprising at least one heteroatom chosen from oxygen, nitrogen, sulfur and halogens.

43. (Previously Presented) The composition according to claim 35, wherein said at least one cationic surfactant is chosen from quaternary ammonium salts of formula (IV) wherein in (ii); R_1 and R_2 , of formula (IV), which may be identical or different, are chosen from aliphatic groups comprising from 1 to 4 carbon atoms and chosen from alkyl groups, alkoxy groups, alkylamide groups and hydroxyalkyl groups.

44. (Previously Presented) The composition according to claim 35, wherein said at least one cationic surfactant is chosen from quaternary ammonium salts of formula (IV) wherein in (ii), at least one of R_3 and R_4 , of formula (IV), which may be identical or different, is chosen from $(C_{12}-C_{22})$ alkylamido (C_2-C_6) alkyl groups and $(C_{12}-C_{22})$ alkyl acetate groups.

45. (Previously Presented) The composition according to claim 35, wherein said at least one cationic surfactant is a quaternary ammonium salt of imidazolinium of formula (V):



wherein R_5 of formula (V) is chosen from alkenyl groups comprising from 8 to 30 carbon atoms and alkyl groups comprising from 8 to 30 carbon atoms, R_6 of formula (V) is chosen from hydrogen, C_1 - C_4 alkyl groups, alkenyl groups comprising from 8 to 30 carbon atoms, and alkyl groups comprising from 8 to 30 carbon atoms, R_7 of formula (V) is chosen from C_1 - C_4 alkyl groups, R_8 of formula (V) is chosen from hydrogen and C_1 - C_4 alkyl groups, and X^- of formula (V) is an anion chosen from halide anions, phosphate anions, acetate anions, lactate anions, alkyl sulfate anions, alkyl sulfonate anions and alkylaryl sulfonate anions.

46. (Previously Presented) The composition according to claim 45, wherein in said formula (V), R_5 of formula (V) is chosen from alkenyl groups comprising from 8 to 30 carbon atoms and alkyl groups comprising from 8 to 30 carbon atoms, wherein said alkenyl groups and alkyl groups are derived from tallow fatty acids.

47. (Previously Presented) The composition according to claim 45, wherein said at least one cationic surfactant is the quaternary diammonium salt propanetallowdiammonium dichloride.

48. (Previously Presented) The composition according to claim 19, wherein said at least one cationic surfactant is chosen from behenyltrimethylammonium salts, stearamidopropyl dimethyl (myristyl acetate) ammonium salts, Quaternium-27 and Quaternium-83.

49. (Previously Presented) The composition according to claim 19, wherein said at least one cationic surfactant is present at a concentration ranging from 0.2% to 10% by weight, relative to the total weight of the composition.

50. (Previously Presented) The composition according to claim 49, wherein said at least one cationic surfactant is present at a concentration ranging from 0.5% to 5% by weight, relative to the total weight of the composition.

51. (Previously Presented) The composition according to claim 50, wherein said at least one cationic surfactant is present at a concentration ranging from 1% to 3.5% by weight, relative to the total weight of the composition.

52. (Previously Presented) The composition according to claim 19, wherein said cosmetically acceptable aqueous medium is chosen from water and a mixture of water and at least one cosmetically acceptable solvent.

53. (Previously Presented) The composition according to claim 52, wherein said cosmetically acceptable solvents are chosen from monoalcohols, polyalcohols, and glycol ethers.

54. (Previously Presented) The composition according to claim 19, further comprising at least one additive chosen from thickeners, perfumes, pearlescent agents, surfactants, preservatives, sunscreens, silicones, anionic polymers, nonionic polymers, cationic polymers, amphoteric polymers, proteins, protein

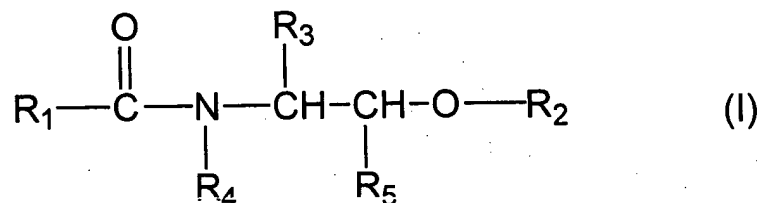
hydrolysates, fatty acids, fatty alcohols, fatty esters, hydroxy acids, vitamins, provitamins, panthenol, vegetable oils, animal oils, mineral oils, and synthetic oils.

55. (Previously Presented) The composition according to claim 54, wherein said at least one additive is a C₁₆-C₄₀ fatty acid chosen from 18-methyleicosanoic acid.

56. (Previously Presented) The composition according to claim 19, wherein said composition is in the form of a composition chosen from: a shampoo; a leave-in conditioner; a rinse-out conditioner; compositions for at least one of permanent waving hair, straightening hair, dyeing hair and bleaching hair; a rinse-out composition to be applied before or after shampooing hair, dyeing hair, bleaching hair, permanent waving hair or hair straightening, or between two stages of permanent waving hair or hair straightening; and a leave-in composition for holding a hair style, for hair shaping or for hair styling.

57. (Previously Presented) A method of making a composition to be applied to the hair, comprising combining, in a cosmetically acceptable aqueous medium, at least one liquid fatty alcohol, at least one ceramide compound and at least one cationic surfactant.

58. (Previously Presented) The method according to claim 57, wherein said at least one ceramide compound is of formula (I):



wherein:

- R₁ is chosen from:

- a saturated or unsaturated, linear or branched, C₁-C₅₀ hydrocarbon group, wherein said C₁-C₅₀ hydrocarbon group is optionally substituted with at least one hydroxyl group, wherein said hydroxyl group is optionally esterified by an acid R₇COOH, R₇ being chosen from a linear or branched, saturated or unsaturated, C₁-C₃₅ hydrocarbon group, wherein said C₁-C₃₅ hydrocarbon group of R₇ is optionally substituted with at least one hydroxyl group that is optionally esterified by a linear or branched, saturated or unsaturated, C₁-C₃₅ fatty acid, wherein said C₁-C₃₅ fatty acid is optionally substituted with at least one hydroxyl group;

- a group R''-(NR-CO)-R', wherein R is chosen from hydrogen and a C₁-C₂₀ hydrocarbon group substituted with at least one hydroxyl group, and wherein R' and R'' are chosen from hydrocarbon groups, wherein the sum of the carbon atoms in R' and R'' ranges from 9 to 30, and wherein R' is a divalent radical; and

- a group R₈-O-CO-(CH₂)_p, wherein R₈ is a C₁-C₂₀ hydrocarbon group, and p is an integer ranging from 1 to 12;

- R_2 is chosen from hydrogen, a saccharide group, a sulfate residue, a phosphate residue, a phosphorylethylamine group and a phosphorylethylammonium group;
- R_3 is chosen from hydrogen and a saturated or unsaturated, linear or branched, C_2 - C_{33} hydrocarbon group, wherein said C_1 - C_{33} hydrocarbon group is optionally substituted with at least one hydroxyl group, wherein said hydroxyl group is
 - optionally esterified by an acid chosen from an inorganic acid and an acid R_7COOH , wherein R_7 has the same meaning as above, or
 - optionally etherified by a group chosen from a (glycosyl) $_n$ group, a (galactosyl) $_m$ group, a sulfogalactosyl group, a phosphorylethylamine group and a phosphorylethylammonium group, wherein n is an integer ranging from 1 to 4 and m is an integer ranging from 1 to 8 ,and wherein R_3 is optionally substituted with at least one C_1 - C_{14} alkyl group;
- R_4 is chosen from hydrogen, a methyl group, an ethyl group, an optionally hydroxylated, linear or branched, saturated or unsaturated, C_3 - C_{50} hydrocarbon group, a group $-CH_2-CHOH-CH_2-O-R_6$, wherein R_6 is chosen from a C_{10} - C_{26} hydrocarbon group and a group $R_8-O-CO-(CH_2)_p$, wherein R_8 is a C_1 - C_{20} hydrocarbon group, and p is an integer ranging from 1 to 12;
- R_5 is chosen from hydrogen and a saturated or unsaturated, linear or branched, C_1 - C_{33} hydrocarbon group optionally substituted with at least one hydroxyl group, wherein said hydroxyl group is optionally etherified by a group chosen from a (glycosyl) $_n$ group, a (galactosyl) $_m$ group, a sulfogalactosyl group, a phosphorylethylamine group, and a phosphorylethylammonium group, wherein m and n have the same meanings as above; and

with the proviso that when R_3 and R_5 are each hydrogen or when R_3 is hydrogen and R_5 is a methyl group, then R_4 is not chosen from hydrogen, a methyl group, and an ethyl group.

59. (Previously Presented) The method according to claim 57, wherein said at least one ceramide compound is chosen from:

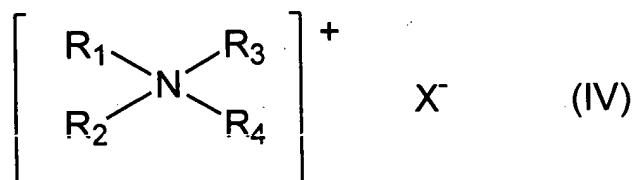
- 2-(N-linoleoylamino)-1,3-octadecanediol,
- 2-(N-oleoylamino)-1,3-octadecanediol,
- 2-(N-palmitoylamino)-1,3-octadecanediol,
- 2-(N-stearoylamino)-1,3-octadecanediol,
- 2-(N-behenoylamino)-1,3-octadecanediol,
- 2-[N-(2-hydroxypalmitoyl)amino]-1,3-octadecanediol,
- 2-(N-stearoylamino)-1,3,4-octadecanetriol, and
- 2-(N-palmitoylamino)-1,3-hexadecanediol.

60. (Previously Presented) The method according to claim 57, wherein said at least one ceramide compound is chosen from bis(N-hydroxyethyl-N-cetyl)malonamide, N-(2-hydroxyethyl)-N-(3-cetyloxy-2-hydroxypropyl)amide of cetylic acid and N-docosanoyl-N-methyl-D-glucamine.

61. (Previously Presented) The method according to claim 57, wherein said at least one liquid fatty alcohol is chosen from lauryl alcohol, isomyristyl alcohol, isostearyl alcohol, isocetyl alcohol, isoarachidyl alcohol, 2-octyldodecanol, 2-butyloctanol and oleyl alcohol.

62. (Previously Presented) The method according to claim 57, wherein said at least one cationic surfactant is chosen from:

A) quaternary ammonium salts of formula (IV):



wherein X^- of formula (IV) is an anion chosen from halide anions, (C₂-C₆)alkyl sulfate anions, phosphate anions, alkyl sulfonate anions, alkylaryl sulfonate anions, and anions derived from an organic acid, and

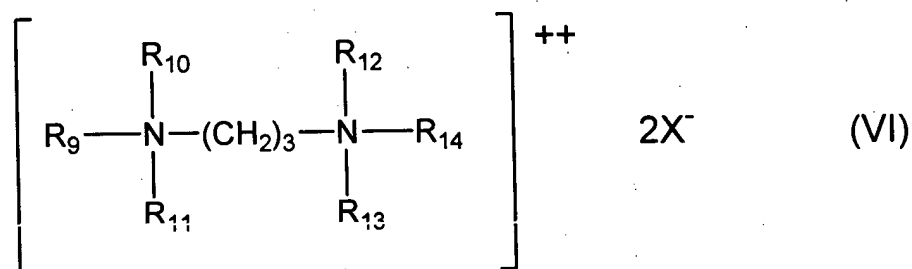
(i) R_1 , R_2 , and R_3 , of formula (IV), which may be identical or different, are chosen from aromatic groups and from linear and branched aliphatic groups comprising from 1 to 4 carbon atoms, wherein said aliphatic groups optionally comprise at least one heteroatom, and then

R_4 of formula (IV) is chosen from linear and branched alkyl groups comprising from 20 to 30 carbon atoms; or alternatively

(ii) R_1 and R_2 , of formula (IV), which may be identical or different, are chosen from aromatic groups and from linear and branched aliphatic groups comprising from 1 to 4 carbon atoms, wherein said aliphatic groups optionally comprise at least one heteroatom, and then

R_3 and R_4 , of formula (IV), which may be identical or different, are chosen from linear and branched alkyl groups comprising from 12 to 30 carbon atoms, wherein said alkyl groups comprise at least one group chosen from ester groups and amide groups;

- B) - quaternary ammonium salts of imidazolinium;
C) - quaternary diammonium salts of formula (VI):



wherein

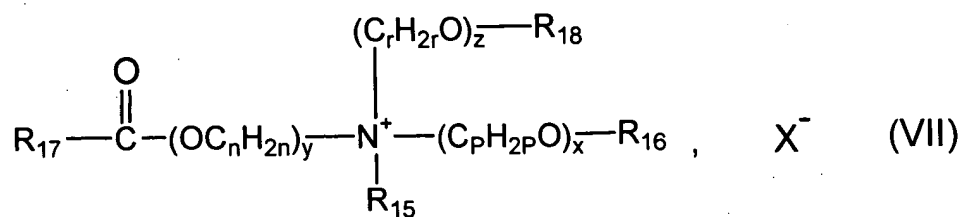
R₉ is chosen from aliphatic groups comprising from about 16 to 30 carbon atoms,

R₁₀, R₁₁, R₁₂, R₁₃ and R₁₄, which may be identical or different, are chosen from hydrogen and alkyl groups comprising from 1 to 4 carbon atoms, and

X⁻ of formula (VI) is an anion chosen from halide anions, acetate anions, phosphate anions, nitrate anions and methyl sulfate anions;

and

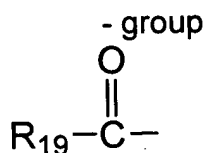
- D) - quaternary ammonium salts, comprising at least one ester functional group, of formula (VII),:



wherein

- R₁₅ is chosen from C₁-C₆ alkyl groups, C₁-C₆ hydroxyalkyl groups, and dihydroxyalkyl groups;

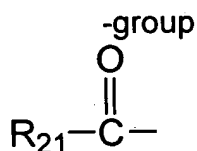
- R₁₆ is chosen from:



- linear and branched, saturated and unsaturated, C₁-C₂₂ hydrocarbon groups R₂₀, and

- hydrogen,

- R₁₈ is chosen from:



- linear and branched, saturated and unsaturated, C₁-C₆ hydrocarbon groups R₂₂, and

- hydrogen,

- R₁₇, R₁₉ and R₂₁, which are identical or different, are each chosen from linear and branched, saturated and unsaturated, C₇-C₂₁ hydrocarbon groups;

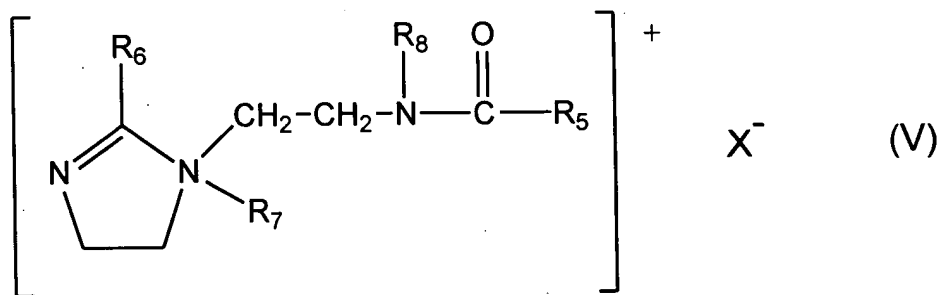
- n, p and r, of formula (VII), which are identical or different, are each integers having values ranging from 2 to 6;

- y of formula (VII) is an integer having a value ranging from 1 to 10;

- x and z, of formula (VII), which are identical or different, are each integers having values ranging from 0 to 10;

- X^- of formula (VII) is an anion chosen from organic anions and inorganic anions, and chosen from simple anions and complex anions;
 with the provisos that the sum $x + y + z$, of formula (VII), has a value ranging from 1 to 15, that when x of formula (VII) has a value of 0, then R_{16} denotes R_{20} , and that when z of formula (VII) has a value of 0, then R_{18} denotes R_{22} .

63. (Previously Presented) The method according to claim 62, wherein said at least one cationic surfactant is a quaternary ammonium salt of imidazolium of formula (V):

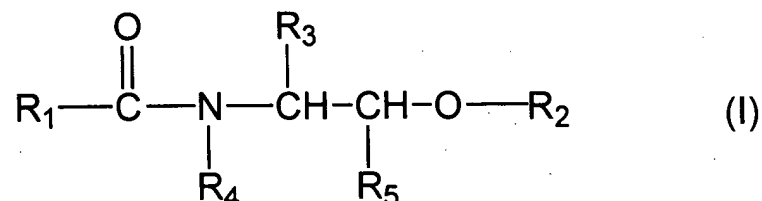


wherein R_5 of formula (V) is chosen from alkenyl groups comprising from 8 to 30 carbon atoms and alkyl groups comprising from 8 to 30 carbon atoms, R_6 of formula (V) is chosen from hydrogen, C_1 - C_4 alkyl groups, alkenyl groups comprising from 8 to 30 carbon atoms, and alkyl groups comprising from 8 to 30 carbon atoms, R_7 of formula (V) is chosen from C_1 - C_4 alkyl groups, R_8 of formula (V) is chosen from hydrogen and C_1 - C_4 alkyl groups, and X^- of formula (V) is an anion chosen from halide anions, phosphate anions, acetate anions, lactate anions, alkyl sulfate anions, alkyl sulfonate anions and alkylaryl sulfonate anions.

64. (Previously Presented) A method for treating keratinous materials, comprising applying at least one composition to said keratinous materials, and then optionally rinsing with water, wherein said at least one composition comprises, in a cosmetically acceptable aqueous medium, at least one liquid fatty alcohol, at least one ceramide compound and at least one cationic surfactant.

65. (Previously Presented) The method according to claim 64, wherein said keratinous materials are chosen from hair.

66. (Previously Presented) The method according to claim 64, wherein said at least one ceramide compound is of formula (I):



wherein:

- R₁ is chosen from:

- a saturated or unsaturated, linear or branched, C₁-C₅₀ hydrocarbon group, wherein said C₁-C₅₀ hydrocarbon group is optionally substituted with at least one hydroxyl group, wherein said hydroxyl group is optionally esterified by an acid R₇COOH, R₇ being chosen from a linear or branched, saturated or unsaturated, C₁-C₃₅ hydrocarbon group, wherein said C₁-C₃₅ hydrocarbon group of R₇ is

optionally substituted with at least one hydroxyl group that is optionally esterified by a linear or branched, saturated or unsaturated, C₁-C₃₅ fatty acid, wherein said C₁-C₃₅ fatty acid is optionally substituted with at least one hydroxyl group;

- a group R''-(NR-CO)-R', wherein R is chosen from hydrogen and a C₁-C₂₀ hydrocarbon group substituted with at least one hydroxyl group, and wherein R' and R'' are chosen from hydrocarbon groups, wherein the sum of the carbon atoms in R' and R'' ranges from 9 to 30, and wherein R' is a divalent radical; and

- a group R₈-O-CO-(CH₂)_p, wherein R₈ is a C₁-C₂₀ hydrocarbon group, and p is an integer ranging from 1 to 12;

- R₂ is chosen from hydrogen, a saccharide group, a sulfate residue, a phosphate residue, a phosphorylethylamine group and a phosphorylethylammonium group;

- R₃ is chosen from hydrogen and a saturated or unsaturated, linear or branched, C₂-C₃₃ hydrocarbon group, wherein said C₁-C₃₃ hydrocarbon group is optionally substituted with at least one hydroxyl group, wherein said hydroxyl group is

- optionally esterified by an acid chosen from an inorganic acid and an acid R₇COOH, wherein R₇ has the same meaning as above, or

- optionally etherified by a group chosen from a (glycosyl)_n group, a (galactosyl)_m group, a sulfogalactosyl group, a phosphorylethylamine group and a phosphorylethylammonium group, wherein n is an integer ranging from 1 to 4 and m is an integer ranging from 1 to 8 ,

and wherein R₃ is optionally substituted with at least one C₁-C₁₄ alkyl group;

- R₄ is chosen from hydrogen, a methyl group, an ethyl group, an optionally hydroxylated, linear or branched, saturated or unsaturated, C₃-C₅₀ hydrocarbon

group, a group $-\text{CH}_2\text{-CHOH-CH}_2\text{-O-R}_6$, wherein R_6 is chosen from a $\text{C}_{10}\text{-C}_{26}$ hydrocarbon group and a group $\text{R}_8\text{-O-CO-(CH}_2)_p$, wherein R_8 is a $\text{C}_1\text{-C}_{20}$ hydrocarbon group, and p is an integer ranging from 1 to 12;

- R_5 is chosen from hydrogen and a saturated or unsaturated, linear or branched, $\text{C}_1\text{-C}_{33}$ hydrocarbon group optionally substituted with at least one hydroxyl group, wherein said hydroxyl group is optionally etherified by a group chosen from a (glycosyl) $_n$ group, a (galactosyl) $_m$ group, a sulfogalactosyl group, a phosphorylethylamine group, and a phosphorylethylammonium group, wherein m and n have the same meanings as above; and

with the proviso that when R_3 and R_5 are each hydrogen or when R_3 is hydrogen and R_5 is a methyl group, then R_4 is not chosen from hydrogen, a methyl group, and an ethyl group.

67. (Previously Presented) The method according to claim 64, wherein said at least one ceramide compound is chosen from:

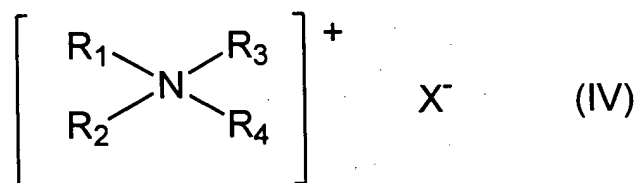
- 2-(N-linoleoylamino)-1,3-octadecanediol,
- 2-(N-oleoylamino)-1,3-octadecanediol,
- 2-(N-palmitoylamino)-1,3-octadecanediol,
- 2-(N-stearoylamino)-1,3-octadecanediol,
- 2-(N-behenoylamino)-1,3-octadecanediol,
- 2-[N-(2-hydroxypalmitoyl)amino]-1,3-octadecanediol,
- 2-(N-stearoylamino)-1,3,4-octadecanetriol, and
- 2-(N-palmitoylamino)-1,3-hexadecanediol.

68. (Previously Presented) The method according to claim 64, wherein said at least one ceramide compound is chosen from bis(N-hydroxyethyl-N-cetyl)malonamide, N-(2-hydroxyethyl)-N-(3-cetyloxy-2-hydroxypropyl)amide of cetylic acid and N-docosanoyl-N-methyl-D-glucamine.

69. (Previously Amended) The method according to claim 64, wherein said at least one liquid fatty alcohol is chosen from lauryl alcohol, isomyristyl alcohol, isostearyl alcohol, isocetyl alcohol, isoarachidyl alcohol, 2-octyldodecanol, 2-butyloctanol and oleyl alcohol.

70. (Previously Presented) The method according to claim 64, wherein said at least one cationic surfactant is chosen from:

A) quaternary ammonium salts of formula (IV):



wherein X^- of formula (IV) is an anion chosen from halide anions, (C_2-C_6) alkyl sulfate anions, phosphate anions, alkyl sulfonate anions, alkylaryl sulfonate anions, and anions derived from an organic acid, and

(i) R_1 , R_2 , and R_3 , of formula (IV), which may be identical or different, are chosen from aromatic groups and from linear and branched aliphatic groups

comprising from 1 to 4 carbon atoms, wherein said aliphatic groups optionally comprise at least one heteroatom, and then

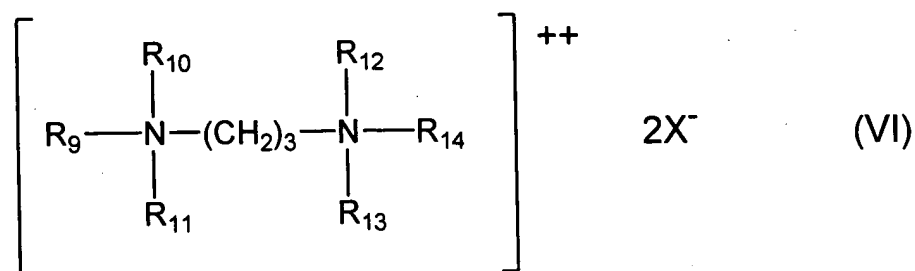
R₄ of formula (IV) is chosen from linear and branched alkyl groups comprising from 20 to 30 carbon atoms; or alternatively

(ii) R₁ and R₂, of formula (IV), which may be identical or different, are chosen from aromatic groups and from linear and branched aliphatic groups comprising from 1 to 4 carbon atoms, wherein said aliphatic groups optionally comprise at least one heteroatom, and then

R₃ and R₄, of formula (IV), which may be identical or different, are chosen from linear and branched alkyl groups comprising from 12 to 30 carbon atoms, wherein said alkyl groups comprise at least one group chosen from ester groups and amide groups;

B) - quaternary ammonium salts of imidazolinium;

C) - quaternary diammonium salts of formula (VI):



wherein

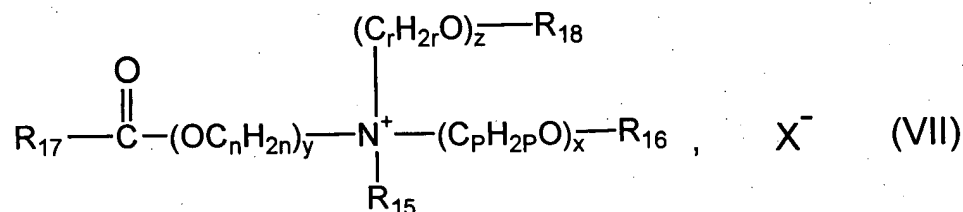
R₉ is chosen from aliphatic groups comprising from about 16 to 30 carbon atoms,

R_{10} , R_{11} , R_{12} , R_{13} and R_{14} , which may be identical or different, are chosen from hydrogen and alkyl groups comprising from 1 to 4 carbon atoms, and

X^- of formula (VI) is an anion chosen from halide anions, acetate anions, phosphate anions, nitrate anions and methyl sulfate anions;

and

D) - quaternary ammonium salts, comprising at least one ester functional group, of formula (VII),:

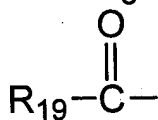


wherein

- R_{15} is chosen from C_1 - C_6 alkyl groups, C_1 - C_6 hydroxyalkyl groups, and dihydroxyalkyl groups;

- R_{16} is chosen from:

- group

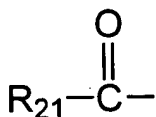


- linear and branched, saturated and unsaturated, C_1 - C_{22} hydrocarbon groups R_{20} , and

- hydrogen,

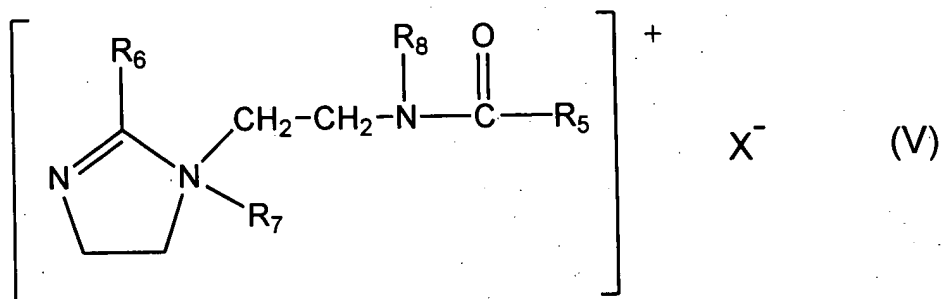
- R_{18} is chosen from:

-group



- linear and branched, saturated and unsaturated, C₁-C₆ hydrocarbon groups
 - R₂₂, and
 - hydrogen,
 - R₁₇, R₁₉ and R₂₁, which are identical or different, are each chosen from linear and branched, saturated and unsaturated, C₇-C₂₁ hydrocarbon groups;
 - n, p and r, of formula (VII), which are identical or different, are each integers having values ranging from 2 to 6;
 - y of formula (VII) is an integer having a value ranging from 1 to 10;
 - x and z, of formula (VII), which are identical or different, are each integers having values ranging from 0 to 10;
 - X⁻ of formula (VII) is an anion chosen from organic anions and inorganic anions, and chosen from simple anions and complex anions;
- with the provisos that the sum x + y + z, of formula (VII), has a value ranging from 1 to 15, that when x of formula (VII) has a value of 0, then R₁₆ denotes R₂₀, and that when z of formula (VII) has a value of 0, then R₁₈ denotes R₂₂.

71. (Previously Presented) The method according to claim 70, wherein said at least one cationic surfactant is a quaternary ammonium salt of imidazolinium of formula (V):



wherein R₅ of formula (V) is chosen from alkenyl groups comprising from 8 to 30 carbon atoms and alkyl groups comprising from 8 to 30 carbon atoms, R₆ of formula (V) is chosen from hydrogen, C₁-C₄ alkyl groups, alkenyl groups comprising from 8 to 30 carbon atoms, and alkyl groups comprising from 8 to 30 carbon atoms, R₇ of formula (V) is chosen from C₁-C₄ alkyl groups, R₈ of formula (V) is chosen from hydrogen and C₁-C₄ alkyl groups, and X⁻ of formula (V) is an anion chosen from halide anions, phosphate anions, acetate anions, lactate anions, alkyl sulfate anions, alkyl sulfonate anions and alkylaryl sulfonate anions.

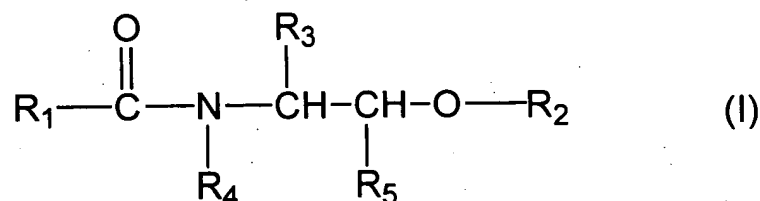
72. (Previously Presented) The method for treating of keratinous materials according to claim 64, wherein said treating is chosen from: a shampooing; conditioning; dyeing; bleaching; permanent waving; and straightening.

73. (Previously Presented) The method for treating of keratinous materials according to claim 64, wherein said at least one composition is applied to said keratinous materials before or after treating said keratinous materials.

74. (Previously Presented) A method of protecting keratinous materials from physical or chemical attacks, comprising applying at least one composition to said keratinous materials, wherein said at least one composition comprises, in a cosmetically acceptable aqueous medium, at least one liquid fatty alcohol, at least one ceramide compound and at least one cationic surfactant.

75. (Previously Presented) The method according to claim 74, wherein said keratinous materials are chosen from hair.

76. (Previously Presented) The method according claim 74, wherein said at least one ceramide compound is of formula (I):



wherein:

- R₁ is chosen from:

- a saturated or unsaturated, linear or branched, C₁-C₅₀ hydrocarbon group, wherein said C₁-C₅₀ hydrocarbon group is optionally substituted with at least one hydroxyl group, wherein said hydroxyl group is optionally esterified by an acid R₇COOH, R₇ being chosen from a linear or branched, saturated or unsaturated, C₁-C₃₅ hydrocarbon group, wherein said C₁-C₃₅ hydrocarbon group of R₇ is optionally substituted with at least one hydroxyl group that is optionally esterified by

a linear or branched, saturated or unsaturated, C₁-C₃₅ fatty acid, wherein said C₁-C₃₅ fatty acid is optionally substituted with at least one hydroxyl group;

- a group R''-(NR-CO)-R', wherein R is chosen from hydrogen and a C₁-C₂₀ hydrocarbon group substituted with at least one hydroxyl group, and wherein R' and R'' are chosen from hydrocarbon groups, wherein the sum of the carbon atoms in R' and R'' ranges from 9 to 30, and wherein R' is a divalent radical; and

- a group R₈-O-CO-(CH₂)_p, wherein R₈ is a C₁-C₂₀ hydrocarbon group, and p is an integer ranging from 1 to 12;

- R₂ is chosen from hydrogen, a saccharide group, a sulfate residue, a phosphate residue, a phosphorylethylamine group and a phosphorylethylammonium group;

- R₃ is chosen from hydrogen and a saturated or unsaturated, linear or branched, C₂-C₃₃ hydrocarbon group, wherein said C₁-C₃₃ hydrocarbon group is optionally substituted with at least one hydroxyl group, wherein said hydroxyl group is

- optionally esterified by an acid chosen from an inorganic acid and an acid R₇COOH, wherein R₇ has the same meaning as above, or

- optionally etherified by a group chosen from a (glycosyl)_n group, a (galactosyl)_m group, a sulfogalactosyl group, a phosphorylethylamine group and a phosphorylethylammonium group, wherein n is an integer ranging from 1 to 4 and m is an integer ranging from 1 to 8 ,

and wherein R₃ is optionally substituted with at least one C₁-C₁₄ alkyl group;

- R₄ is chosen from hydrogen, a methyl group, an ethyl group, an optionally hydroxylated, linear or branched, saturated or unsaturated, C₃-C₅₀ hydrocarbon group, a group -CH₂-CHOH-CH₂-O-R₆, wherein R₆ is chosen from a C₁₀-C₂₆

hydrocarbon group and a group $R_8-O-CO-(CH_2)_p$, wherein R_8 is a C_1-C_{20} hydrocarbon group, and p is an integer ranging from 1 to 12;

- R_5 is chosen from hydrogen and a saturated or unsaturated, linear or branched, C_1-C_{33} hydrocarbon group optionally substituted with at least one hydroxyl group, wherein said hydroxyl group is optionally etherified by a group chosen from a (glycosyl) $_n$ group, a (galactosyl) $_m$ group, a sulfogalactosyl group, a phosphorylethylamine group, and a phosphorylethylammonium group, wherein m and n have the same meanings as above; and
with the proviso that when R_3 and R_5 are each hydrogen or when R_3 is hydrogen and R_5 is a methyl group, then R_4 is not chosen from hydrogen, a methyl group, and an ethyl group.

77. (Previously Presented) The method according to claim 74, wherein said at least one ceramide compound is chosen from:

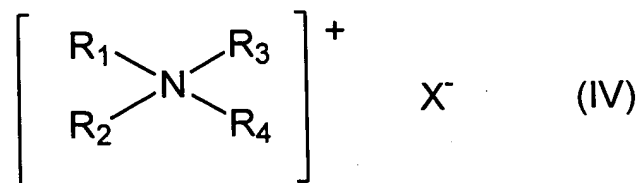
- 2-(N-linoleoylamino)-1,3-octadecanediol,
- 2-(N-oleoylamino)-1,3-octadecanediol,
- 2-(N-palmitoylamino)-1,3-octadecanediol,
- 2-(N-stearoylamino)-1,3-octadecanediol,
- 2-(N-behenoylamino)-1,3-octadecanediol,
- 2-[N-(2-hydroxypalmitoyl)amino]-1,3-octadecanediol,
- 2-(N-stearoylamino)-1,3,4-octadecanetriol, and
- 2-(N-palmitoylamino)-1,3-hexadecanediol.

78. (Previously Presented) The method according to claim 74, wherein said at least one ceramide compound is chosen from bis(N-hydroxyethyl-N-cetyl)malonamide, N-(2-hydroxyethyl)-N-(3-cetyloxy-2-hydroxypropyl)amide of cetylic acid and N-docosanoyl-N-methyl-D-glucamine.

79. (Previously Amended) The method according to claim 74, wherein said at least one liquid fatty alcohol is chosen from lauryl alcohol, isomyristyl alcohol, isostearyl alcohol, isocetyl alcohol, isoarachidyl alcohol, 2-octyldodecanol, 2-butyloctanol and oleyl alcohol.

80. (Previously Presented) The method according to claim 74, wherein said at least one cationic surfactant is chosen from:

A) quaternary ammonium salts of formula (IV):



wherein X^- of formula (IV) is an anion chosen from halide anions, (C_2-C_6) alkyl sulfate anions, phosphate anions, alkyl sulfonate anions, alkylaryl sulfonate anions, and anions derived from an organic acid, and

(i) R_1 , R_2 , and R_3 , of formula (IV), which may be identical or different, are chosen from aromatic groups and from linear and branched aliphatic groups

comprising from 1 to 4 carbon atoms, wherein said aliphatic groups optionally comprise at least one heteroatom, and then

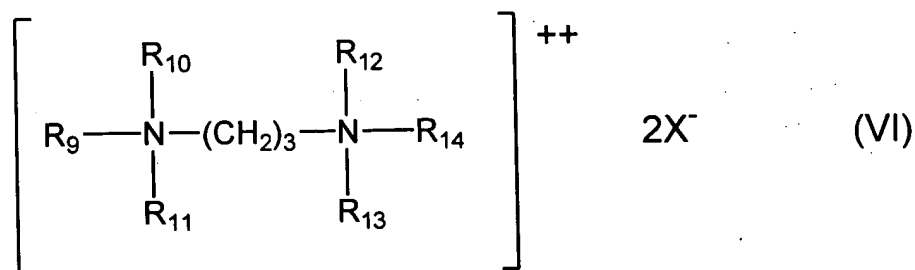
R₄ of formula (IV) is chosen from linear and branched alkyl groups comprising from 20 to 30 carbon atoms; or alternatively

(ii) R₁ and R₂, of formula (IV), which may be identical or different, are chosen from aromatic groups and from linear and branched aliphatic groups comprising from 1 to 4 carbon atoms, wherein said aliphatic groups optionally comprise at least one heteroatom, and then

R₃ and R₄, of formula (IV), which may be identical or different, are chosen from linear and branched alkyl groups comprising from 12 to 30 carbon atoms, wherein said alkyl groups comprise at least one group chosen from ester groups and amide groups;

B) - quaternary ammonium salts of imidazolinium;

C) - quaternary diammonium salts of formula (VI):



wherein

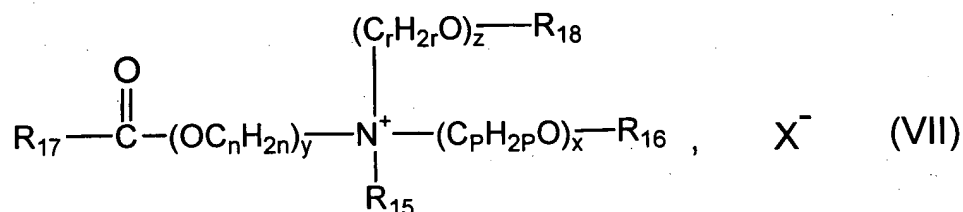
R₉ is chosen from aliphatic groups comprising from about 16 to 30 carbon atoms,

R_{10} , R_{11} , R_{12} , R_{13} and R_{14} , which may be identical or different, are chosen from hydrogen and alkyl groups comprising from 1 to 4 carbon atoms, and

X^- of formula (VI) is an anion chosen from halide anions, acetate anions, phosphate anions, nitrate anions and methyl sulfate anions;

and

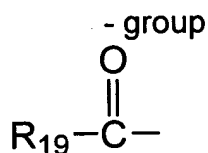
D) - quaternary ammonium salts, comprising at least one ester functional group, of formula (VII),:



wherein

- R_{15} is chosen from C_1 - C_6 alkyl groups, C_1 - C_6 hydroxyalkyl groups, and dihydroxyalkyl groups;

- R_{16} is chosen from:

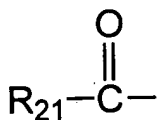


- linear and branched, saturated and unsaturated, C_1 - C_{22} hydrocarbon groups R_{20} , and

- hydrogen,

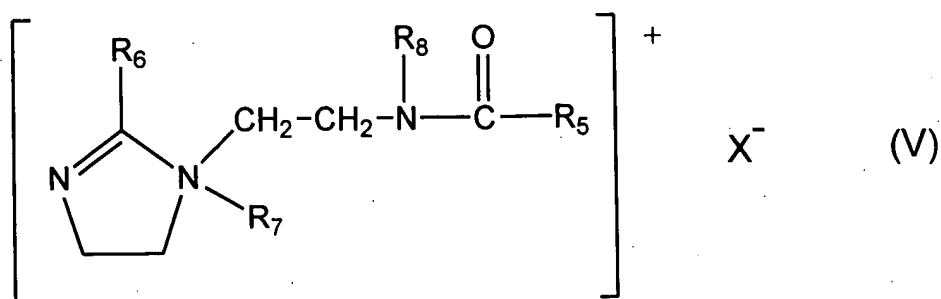
- R_{18} is chosen from:

-group



- linear and branched, saturated and unsaturated, C₁-C₆ hydrocarbon groups
 - R₂₂, and
 - hydrogen,
 - R₁₇, R₁₉ and R₂₁, which are identical or different, are each chosen from linear and branched, saturated and unsaturated, C₇-C₂₁ hydrocarbon groups;
 - n, p and r, of formula (VII), which are identical or different, are each integers having values ranging from 2 to 6;
 - y of formula (VII) is an integer having a value ranging from 1 to 10;
 - x and z, of formula (VII), which are identical or different, are each integers having values ranging from 0 to 10;
 - X⁻ of formula (VII) is an anion chosen from organic anions and inorganic anions, and chosen from simple anions and complex anions;
- with the provisos that the sum x + y + z, of formula (VII), has a value ranging from 1 to 15, that when x of formula (VII) has a value of 0, then R₁₆ denotes R₂₀, and that when z of formula (VII) has a value of 0, then R₁₈ denotes R₂₂.

81. (Previously Presented) The method according to claim 80, wherein said at least one cationic surfactant is a quaternary ammonium salt of imidazolinium of formula (V):



wherein R₅ of formula (V) is chosen from alkenyl groups comprising from 8 to 30 carbon atoms and alkyl groups comprising from 8 to 30 carbon atoms, R₆ of formula (V) is chosen from hydrogen, C₁-C₄ alkyl groups, alkenyl groups comprising from 8 to 30 carbon atoms, and alkyl groups comprising from 8 to 30 carbon atoms, R₇ of formula (V) is chosen from C₁-C₄ alkyl groups, R₈ of formula (V) is chosen from hydrogen and C₁-C₄ alkyl groups, and X⁻ of formula (V) is an anion chosen from halide anions, phosphate anions, acetate anions, lactate anions, alkyl sulfate anions, alkyl sulfonate anions and alkylaryl sulfonate anions.

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Edited by

CHARLES ZVIAK

Chairman and Chief Executive

L'Oréal

Paris, France



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series editors

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Consultant Dermatologist

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London, England

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Department of Dermatology

University of California School of Medicine
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Additional Volumes in Preparation

Other studies include resistance to permanent waving and to synthetic sweat and stability of the dye under accelerated storage conditions (40–50 °C) in a reference vehicle and in comparison with a fresh dye solution.

Oxidation. Dye Precursors. If the new compound is a primary intermediate, it is first tested alone in the presence of an oxidizer. Further oxidation and coupling reactions are then examined, using the main couplers: *meta*-diphenol, *meta*-diamine, *meta*-aminophenol. In the case of a new coupler, the study will first center on oxidative reaction products with the major intermediates: *paraphenylenediamine* (PPD), *para*toluenediamine (PTD), *para*-amino and *ortho*-aminophenols (see Chap. 8).

The assessment protocol is similar to that mentioned above for direct dyes. The criteria are the dyeing power, selectivity, resistance to repeated washing, light, weathering, and so forth.

If the new dye succeeds in passing this first series of assays, it is tested in varying vehicles. For an oxidation dye, the investigations will be extended to all the possible couplings. This stage aims at defining the potential area of development for the product. Preformulation tests are then possible, and more complex formulations are produced to obtain typical shades.

Testing is done first on swatches of hair and then on human heads, once safety is guaranteed by toxicological studies. At the same time, long-term storage in typical packaging will be carried out in detail, as are resistance to washing, sunlight, etc. using formulations that are almost ready to be marketed.

In Vivo Studies

In a number of cases metrological methods *in vitro* are not suitable for selecting ingredients in accordance with the desired properties. Other methods must be applied.

Antidandruff Agents. In so far as the criterion chosen for activity [25] is growth inhibition of specific strains of microorganisms, e.g., *Pityrosporum genus*, screening will be carried out using suitable bacteriological techniques. They determine the minimum concentration exerting an inhibitory effect on bacteria and yeasts whose proliferation is associated with dandruff conditions.

Anisobortheic Agents. To select this type of ingredient, whose action is aimed at the scalp level, biological techniques were developed in different research centers, either on isolated organs or *in vivo* on animals. Among them are the following:

1. Tests on animals fed deficient diets [26,27]: Animals (rats) are given a diet lacking in biotin and pyridoxine, which creates a seborrheic conditions. Hyper trophy and hyperplasia of the sebaceous glands occur, accompanied by increased lipid excretion at the skin surface, giving a very greasy aspect to the hair.
2. Tests on animals given androgens: Rats or hamsters are used, male or female, castrated or noncastrated. They receive suitably controlled doses of

testosterone intramuscularly or subcutaneously. The volume of the sebaceous glands is markedly increased, and a greasy condition is produced [28,29].

In both cases the animals are conditioned over a period of 2–3 weeks. They are divided into two groups, one being a control group. After a defined treatment period using the ingredients under test, the effect on the number and size of sebaceous glands and the production of sebum is evaluated.

Histological techniques are employed to visualize and measure the effects on the sebaceous glands. Lipid biosynthesis can be followed by biochemical analyses using ¹⁴C-labeled precursors (glucose or sodium acetate) [30a,b]. The amount of sebum excreted is assessed either by solvent extraction techniques [31] or a photometric method (discussed in Sec. III, E).

III. TESTS ON FINISHED PRODUCTS

A. Safety

General Approach

All finished cosmetic products must be evaluated for safety in use to make sure that they do not, under normal and foreseeable conditions, constitute a potential hazard for the consumer. Most countries have provided regulations for such testing. Ingredients can be used in a variety of finished products. It might seem that a sensible way of proceeding would be to conduct most toxicological tests on the ingredients, which would reduce the amount of experimentation and cost of developing finished products. However, experience has shown that the formula-tion itself is the important element. It determines local tolerance after a single or repeated application, eye and/or lung mucosa tolerance, the degree of absorption through the skin, etc.

Apart from the effects of the vehicle, it has been observed that the association of different compounds can produce either synergistic toxicity or, on the contrary, a mitigation or even inhibition of toxic effects.

Another basic fact that must be kept in mind is that some compounds may undergo chemical modification when used. This is the case with oxidation dyes, for example, which are mixed with an oxidizer in an alkaline vehicle prior to use. Dilution at the time of use is another factor to consider; it is capable of modifying adverse effects to a notable extent.

It is difficult to set up fixed protocols for safety evaluation, because exposure can vary considerably between products, and a rigid protocol would not be appropriate for all products. In all cases the bulk of the testing will focus on tolerance. In some cases, additional testing might be necessary: when totally new ingredients are used, or known ingredients whose physicochemical characteristics have been changed as a result of formulation, or ingredients whose absorption

rate may be significantly altered by the vehicle or by previous hair treatments, or ingredients belonging to a class of compound under suspicion from a toxicological standpoint.

The toxicological profile of a product must be established in accordance with its anticipated use. This is of prime importance. It is unrealistic to establish a single list of tests to be performed on all categories of product. Some tests are common for all products, but specific tests must be introduced according to a product's intended use. An interesting approach to this problem has been developed in France by the Ministry of Health (see Appendix).

If the product under test belongs to a homologous series—as in the case of a dye formula, which may include up to 60 shades—safety tests will be performed on typical products containing all the ingredients at the maximum usage concentration in a product.

The interpretation of test results should take into consideration all the accumulated human experience with respect to products on the market for years without producing untoward side effects. For this reason, scientists try to range the product safety in comparison with reference products of similar nature and identical use, whenever possible.

Common Safety Tests

The methods are described above in the section on ingredients. In addition to acute oral toxicity, carried out to determine the consequences of accidental ingestion, local tolerance is the most important criterion. It is necessary to determine the product's potential to induce irritation in skin and mucosa after single or repeated applications, taking actual conditions and frequency of use into account, as well as the sensitizing potential.

Specific Tests

Inhalation. This is a concern for products sold in aerosol form. The studies are carried out in a glass or stainless steel chamber in which the product is sprayed so as to reach the desired concentrations in the atmosphere. The animals (rats) are placed in these chambers for six hours. They are allowed to move freely, and this favors product inhalation.

Acute toxicity is determined by observing the mortality rate during 14 days after exposure; similarly, the toxicity of cumulative doses through successive exposures is assessed [32a, b]. Hematologic analyses, macroscopic and microscopic examinations of the viscera and different parts of the respiratory system, and especially a histological study of the nasal cavity, trachea, and lung, are performed.

Percutaneous Toxicity. Most hair products come into contact with the scalp for a relatively short time. They are applied and then rinsed out. The probability of their being absorbed is therefore extremely small (see Chap. 9). This leads to

the question as to whether it is necessary to determine the percutaneous toxicity. Bourinnet states that "percutaneous toxicity studies are only exceptionally required" [33].

It is up to the scientist to decide if there should be additional tests on the basis of the product composition, the available toxicological data for new ingredients, and the results of the tests previously mentioned. Should they be needed, percutaneous toxicity tests on finished products would involve the following:

1. Single application toxicity: Rats or rabbits are used. They are first shaved (sides and back), and the product is applied directly to the skin. The application zone remains covered for 24 hr. The LD50 expressed in mg/kg is determined.
2. Subacute toxicity: The product is applied daily, at three concentrations, to rabbits for a 4-week period following procedures similar to those described above. The assessment includes weight change and clinical follow-up, biological analyses and histopathological studies.

Human Data

There are obvious ethical reasons preventing the use of human beings for testing. However, observations made on people are of prime importance, because extrapolating data from animals to human beings is difficult. Information on the irritation and sensitization potential of the finished product would be of major interest.

The techniques employed are dealt with in a separate chapter (Chap. 12) and will not be discussed here.

B. Microbial Contamination

One of the requisites that must be met before a product can be marketed is the absence of contamination by microorganisms. It must not contain any pathogenic organisms, or organisms that might lead to physical, chemical, or toxicological alterations rendering the product unsuitable for use.

It is difficult to define either quantitative or qualitative standards for saprophytes present in the environment, in particular for products to be used on the scalp, a germ-rich area.

Formulation is normally carried out so as to develop a product with low bacterial contamination that can be maintained from manufacture to consumer use. Action is taken at two levels: limiting the initial contamination, and limiting further contamination at the time of use.

The finished product must include one or several appropriate preservatives. The choice of preservative is complicated, for it must achieve the following:

1. Be effective against a wide range of microorganisms
2. Retain a constant level of activity
3. Be compatible with the composition